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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HEINCER, LIAM J	

ART UNIT	PAPER NUMBER
1796	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/576,038	MAYNARD ET AL.	
	Examiner	Art Unit	
	Liam J. Heincer	1796	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *15-19* is/are allowed.

6)☒ Claim(s) *1-14 and 20-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 30, 2009 has been entered.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Gololobov et al. (US Pat. 6,433,078).

Considering Claims 1 and 21: Gololobov et al. teaches a method for forming a polymer-enyzme/biomacromolecule conjugate (4:19-23) comprising reacting a monomer (4:45-21) with sites on the enzyme modified to include polymerization initiation sites (4:36-43). The method of Golobov et al. results in products with one biomolecule attached to one or more polymer chains (Example 6).

Considering Claims 2 and 3: Gololobov et al. teaches the enzyme/protien as having amino acids (4:36-43).

Considering Claim 5: Gololobov et al. teaches filtering the conjugate/removing unreacted starting materials (8:43-47).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gololobov et al. (US Pat. 6,433,078) as applied to claim 3 above, and further in view of Matyjaszewski et al. (US 5,789,487).

Considering Claims 1-4 and 21: Gololobov et al. teaches a method for forming a polymer-enyzme/biomacromolecule conjugate (4:19-23) comprising reacting a monomer (4:45-21) with sites on the enzyme modified to include polymerization initiation sites (4:36-43). The method of Golobov et al. results in products with one biomolecule attached to one or more polymer chains (Example 6). Gololobov et al. teaches the enzyme/protein as having amino acids (4:36-43).

Gololobov et al. does not teach the modified polymerisazition site as being an initiator. However, Matyjaszewski et al. teaches an atom transfer radical polymerization initiator as being attached to a macromolecule (17:25-59). Gololobov et al. and Matyjaszewski et al. are combinable as they are concerned with a similar technical difficulty, namely grafting acrylate monomers onto a macromolecule. It would have been obvious to a person having ordinary skill in the art at the time of invention to have used the initator of Matyjaszewski et al. as the polymerization site of Gololobov et al., and the motivation to do so would have been, as Matyjaszewski et al. suggests, atom transfer radical polymerization has a uniform growth on all chains (4:60-5:9).
Considering Claim 5: Gololobov et al. teaches filtering the conjugate/removing unreacted starting materials (8:43-47).

Claims 6 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gololobov et al. (US Pat. 6,433,078) in view of Matyjaszewski et al. (US 5,789,487).as applied to claim 4 above, and further in view of Kroner et al. (US Pat. 5,260,396).
Considering Claims 6 and 7: Gololobov et al. and Matyjaszewski et al. collectively teach the method of claim 4 as shown above.

Gololobov et al. does not teach adding a non-interacting initiator to the composition. However, Kroner et al. teaches adding a insoluble initiator during a protein-ethylnically unsaturated monomer based polymer graft copolymer synthesis to remove residual monomers at the beginning of the polymerization reaction (4:53-63). Gololobov et al. and Kroner et al. are analogous art as they are concerned with the same field of endeavor, namely graft polymerization of unsaturated monomers onto proteins. It would have been obvious to a person having ordinary skill in the art at the time of invention to have used the initiator of Kroner et al. in the process of Gololobov et al., and the motivation to do so would have been, as Kroner et al. suggests, to remove unreacted monomers (4:53-63).

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gololobov et al. (US Pat. 6,433,078) in view of Matyjaszewski et al. (US 5,789,487).

Considering Claim 8: Gololobov et al. teaches a method for forming a polymer-enyzme/protein conjugate (4:19-23) comprising reacting a monomer (4:45-21) with sites on the enzyme modified to include reactive sites (4:36-43).

Gololobov et al. does not teach the modified polymerisazition site as being an initiator. However, Matyjaszewski et al. teaches an atom transfer radical polymerization initiator as being attached to a macromolecule (17:25-59). Gololobov et al. and Matyjaszewski et al. are combinable as they are concerned with a similar technical difficulty, namely grafting acrylate monomers onto a macromolecule. It would have been obvious to a person having ordinary skill in the art at the time of invention to have used the initator of Matyjaszewski et al. as the polymerization site of Gololobov et al., and the motivation to do so would have been, as Matyjaszewski et al. suggests, atom transfer radical polymerization has a uniform growth on all chains (4:60-5:9).

Claims 9, 10, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gololobov et al. (US Pat. 6,433,078) in view of Matyjaszewski et al. (US 5,789,487).

Considering Claims 9 and 10: Gololobov et al. teaches a method for forming a polymer-enyzme/protein conjugate (4:19-23) comprising reacting a monomer (4:45-21) with sites on the enzyme modified to include vinyl groups/functionality for radical initiation (4:36-43).

Gololobov et al. does not teach the modified polymerisazition site as being an initiator. However, Matyjaszewski et al. teaches an atom transfer radical polymerization initiator as being attached to a macromolecule (17:25-59). Gololobov et al. and Matyjaszewski et al. are combinable as they are concerned with a similar technical difficulty, namely grafting acrylate monomers onto a macromolecule. It would have been obvious to a person having ordinary skill in the art at the time of invention to have used the initator of Matyjaszewski et al. as the polymerization site of Gololobov et al., and the motivation to do so would have been, as Matyjaszewski et al. suggests, atom transfer radical polymerization has a uniform growth on all chains (4:60-5:9).

Considering Claims 13: Gololobov et al. teaches the monomer as being N-isopropylacrylamide.

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gololobov et al. (US Pat. 6,433,078) in view of Matyjaszewski et al. (US 5,789,487)as applied to claim 9 above, in view of Jansen et al. (US Pat. 4,980,457).
Considering Claim 14: Gololobov et al. and Matyjaszewski et al. collectively teach the method of claim 9 as shown above. Gololobov et al. also teaches the monomer as being N-isopropylacrylamide.

Gololobov et al. does not teach attaching the functional group through the propyl mecrapto pyridine group of the instant claim. However, Jansen et al. teaches attaching functional groups to a polymer through a disulfide group activated by a pyridine group. Gololobov et al. and Jansen et al. are combinable as they are concerned with a similar technical difficulty, namely functionalizing proteins. It would have been obvious to a person having ordinary skill in the art at the time of invention to have used the activated disulfide of Jansen et al. in the method of Gololobov et al., and the motivation to do so would have been, as Jansen et al. suggests, to allow the functionalizing agent to reacted with the thiols of the protein.

Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gololobov et al. (US Pat. 6,433,078) in view of Matyjaszewski et al. (US 5,789,487).
Considering Claim 20: Gololobov et al. teaches a polymer-enyzme/protein conjugate (4:19-23) comprising reacting a monomer (4:45-21) with sites on the enzyme modified to include reactive sites (4:36-43).

Gololobov et al. does not teach the modified polymerisazition site as being an initiator. However, Matyjaszewski et al. teaches an atom transfer radical polymerization initiator as being attached to a macromolecule (17:25-59). Gololobov et al. and Matyjaszewski et al. are combinable as they are concerned with a similar technical difficulty, namely grafting acrylate monomers onto a macromolecule. It would have been obvious to a person having ordinary skill in the art at the time of invention to have

used the initator of Matyjaszewski et al. as the polymerization site of Gololobov et al., and the motivation to do so would have been, as Matyjaszewski et al. suggests, atom transfer radical polymerization has a uniform growth on all chains (4:60-5:9).

Claims 22 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gololobov et al. (US Pat. 6,433,078) in view of Matyjaszewski et al. (US 5,789,487) as applied to claims 2 and 21 above, and further in view of Hoffman et al. (US Pat. 5, 988, 588).

Gololobov et al. teaches the method of claims 2 and 21 as shown above.
Considering Claim 22: Gololobov et al. does not teach the enzyme as being lysozyme. However, Hoffman et al. teaches using lysozyme in a polymer-bimolecule conjuage (10:20-25). Gololobov et al. and Hoffman et al. are combinable as they are concerned with the same field of endeavor, namely polymer-enyzme conjugates. It would have been obvious to a person having ordinary skill in the art at the time of invention to have used lysozyme in the conjugate of Gololobov et al. as in Hoffman et al., and the motivation to do so would have been, as Hoffman et al. suggests, lysozyme is pH sensitive, providing a environmentally responsive conjugate (10:20-25).
Considering Claim 23: Gololobov et al. does not teach the biomolecule as being an antibody. However, Hoffman et al. teaches using antibodies in polymer-biomolecule conjugates (3:2-8). It would have been obvious to a person having ordinary skill in the art at the time of invention to have used an antibody in the conjugate of Gololobov et al. as in Hoffman et al., and the motivation to do so would have been, as Hoffman et al. suggests, antibodies are presented as being functionally equivalent to enzymes in the conjugate (3:2-8).

Claims 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bontempo et al. (J. Am. Chem. Soc. 2004, 126, 15372-15373) in view of Matyjaszewski et al. (US 5,789,487).
Considering Claim 11: Bontempo et al. teaches a method of forming a polymer-boimacromolecule conjugate (pg. 15372) by modifying a protein with ATRP initiator that

has been modified with a monomer (pg. 15372). Bontempo et al. also teaches conjugate as having one protein (scheme 1). Bontempo et al. also teaches modifying the protein to provide free cysteines/thiols (pg. 15372).

Bontempo et al. does not teach attaching the initiator to the protein prior to the reaction with the monomer. However, Matyjaszewski et al. teaches an atom transfer radical polymerization initiator as being attached to a macromolecule (17:25-59). Bontempo et al. and Matyjaszewski et al. are analogous art as they are concerned with the same field of endeavor, namely graft polymers based on ATRP polymerization reactions. It would have been obvious to a person having ordinary skill in the art at the time of invention to have reacted the intiator with the protein prior to polymerization in the process of Bontempo et al. as in Matyjaszewski et al., and the motivation to do so would have been, the selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results. *In re Burhans*, 154 F.2d 690, 69 USPQ 330 (CCPA 1946). See MPEP § 2144.04.

Considering Claim 12: Bontempo et al. teaches the intiator as being pyridyl disulfide functional (pg. 15372).

Bontempo et al. does not teach the protein as being reduced with tris-(2-carboxyethyl) phosphine dichloride. However, it is common practice in the art to modify proteins with tris-(2-carboxyethyl) phosphine dichloride to generate free cysteines (applicant's arguments July 28, 2008, page 6). It would have been obvious to a person having ordinary skill in the art at the time of invention to have used this practice to generate the free thiols, and the motivation to do so would have been to generate reactive sites in the polymer.

Bontempo et al. does not teach capping the polymer with maleimide. However, it is common practice to cap free cysteine with maleimide (applicant's arguments July 28, 2008, page 6). It would have been obvious to a person having ordinary skill in the art at the time of invention to have used this practice to cap the free cysteine and the motivation to do so would have been to prevent further reaction of the cysteine.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. See PTO form 892.

Allowable Subject Matter

Claims 15-19 are allowed.

Response to Amendment

The declarations under 37 CFR 1.132 filed March 30, 2009 is sufficient to overcome the rejection of claims 11, 12, and 22 based upon Heredia et al.

Response to Arguments

Applicant's arguments filed March 30, 2009 have been fully considered but they are not persuasive, because:

A) Applicants argument that Gololobov et al. does not teach the production of conjugates containing only one biomacromolecule is not persuasive. While Gololobov et al. teaches that some of the enzymes can crosslink, the crosslinked enzymes are removed from the reaction medium (Example 6). Therefore the process results in conjugates containing only one enzyme.

Addtionally, the method of Matyjaszewski et al. results in polymers where the macromonomer does not react with other macromonomers/ABA polymers (18:43-52). This is different than ABAB… polymers as alleged by the applicant. Therefore, the combination of Gololobov et al. and Matyjaszewski et al. would result in conjugates with only one protein per conjugate. As Gololobov et al. shows clear desire to form polymers with only one protein (Example 6), this provides further motivation to a person having ordinary skill in the art at the time of invention to combine the references.

B) Applicants argument that claims 11 and 12 cannot be rejected without rejecting claim 9 is not persuasive. As explained in the previous action, claims 11 and 12 do not have support in the PCT application, and thus were only given the U.S. filing date as the priority date. As such, Bontempo et al. applies as art for claims 11 and 12 despite being published after the PCT filing date. As all the limtaions of claim 9 have been addressed in the above rejection of claims 11 and 12, the rejection is valid despite the parent's absence from the rejection.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Liam J. Heincer whose telephone number is 571-270-3297. The examiner can normally be reached on Monday thru Friday 7:30 to 5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Eashoo can be reached on 571-272-1197. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mark Eashoo/
Supervisory Patent Examiner, Art Unit 1796

LJH
May 26, 2009